## REMARKS

Claims 1-23 are pending in the above-referenced application. Claim 13 has been cancelled. As will be discussed in further detail below, claims 1, 5, 18 and 19 have been amended to more distinctly claim that which Applicants regard as their invention. The amendments to claims 1, 18 and 19 are supported by the specification; no new matter has been added.

### 1. Priority claim

It is asserted that claims 19, 21 and 23 are not entitled to the priority date of the provisional application because the recited compounds are not adequately described in said application. Applicants respectfully dispute the assertion. In Applicants view, these compounds are adequately described since the specification allows persons of ordinary skill in the art "to recognize that the inventor invented what is claimed". *In re Gostelli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) and the enablement requirement is met by providing a specification that teaches one of ordinary skill in the art "how to make and use the invention as broadly as it is claimed". *In re Goodman*, 11 F.3d 1046, 1050, 29 USPQ2d 2010, 2013 (Fed. Cir. 1993). The compounds of claim 19 are actually encompassed by formula I. For Examiner's reference, Applicants attach hereto as Appendix A, pages 2-4 of the provisional application. Specific species encompassed by claim 19 are highlighted. Furthermore, the enablement requirement is fulfilled since methods were disclosed in the provisional application for obtaining said compounds (see pages 13-16).

### 2. The Rejections Under 35 U.S.C. 112, Second Paragraph

Claims 1-23 have been rejected under 35 U.S.C. 112, second paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as their invention. Four grounds were given. Applicants will respond to each of the grounds below.

**2.1 Recitation of "Comprising"**

It is asserted that the recitation of the phrase "comprising" in the definition of 3-6 membered heterocyclic ring at various places of claim 1 renders the claim indefinite since the term is open-ended and can include more than what is being positively recited therein. It is noted in the Office Action that "comprising" is a term of art used in claim language which means that the named elements are essential but other elements may be added and still form a construct within the scope of the claim.

Applicants respectfully traverse the rejection. The MPEP §2173.04 states

> Breadth of a claim is not to be equated with indefiniteness. *In re Miller*, 441 F.2d 689, 169 USPQ 597 (CCPA 1971). If the scope of the subject matter embraced by the claims is clear, and if applicants have not otherwise indicated that they intend the invention to be of a scope different from that defined in the claims, then the claims comply with 35 U.S.C. 112, second paragraph.

Applicants assert that the scope of claim 1 is certainly clear. For example, claim 1 does adequately set forth what needs to be included in "R1" or "R3". Either R1 or R3 may be a 3-6 membered heterocyclic ring that contains one or more nitrogen, sulfur and/or oxygen atoms. Further, it is stated that the compound of formula I may be obtained from methods (a)-(d). However, it would be evident to one of ordinary skill in the art that additional steps may be included. However, the essential elements are clearly defined. Therefore, claim 1 does comply with 35 U.S.C. 112, second paragraph.

**2.2 Recitation of Prodrug**

It is asserted that the recitation of "prodrug" is indefinite. Applicants respectfully

traverse the rejection. "Prodrug" is clearly defined on page 5 of the specification. However, in order to advance prosecution, the term "prodrug" has been removed from claim 1. Applicants do reserve the right to pursue this cancelled subject matter in subsequently filed continuation and/or divisional applications.

**2.3 Recitation of Metabolite**

It is asserted that the recitation of "metabolite" is indefinite. Applicants respectfully traverse the rejection. "Metabolite" is clearly defined on page 4, lines 32-36 of the specification. However, in order to advance prosecution, the term "prodrug" has been removed from claim 1. Applicants do reserve the right to pursue this cancelled subject matter in subsequently filed continuation and/or divisional applications.

**2.4 Process (d) of claims 1 and 5**

It is asserted that process (d) of claims 1 and 5 is indefinite. Specifically, it is stated

> ...it is not clear what the relevance of definition of X as formula IV' has no X. In addition the X' definition remains unknown in view of the proviso recited in these claims. Note whereas X/ is defined as selected from groups defined for X, the proviso recites X'≠X. Thus it is not clear what is X'.

In response and particularly in order to advance prosecution, claim 1 d) has been amended to recited that (IV) of c) is converted to (IV)' and further that "X" of (IV) is transformed into X'. Additionally, it is stated that X' can be selected from the same substituents as X but should just be different. Furthermore, claim 5 has been amended to show IV. In view of the amendments of claims 1 and 5, Applicants assert that process d) is not indefinite.

**2.5 Claims 18 and 19**

It is asserted that claims 18 and 19 are indefinite since they are recited as a product by process. However, the Examiner asserts that the product is the same whatever the process

by which they are made and that it is not clear what additional limitation is being claimed by the phrase "obtained by the process according to claim 1". In response and particularly in order to advance prosecution, claims 18 and 19 have been amended to remove the phrase "obtained by the process according to claim 1".

In view of the above arguments and amendments, Applicants assert that the rejections of claims 1-23 under 35 U.S.C. 112, second paragraph have been overcome. Therefore, Applicants respectfully request that the rejection be withdrawn.

**4. The Rejection Under 35 U.S.C. 102**

Claims 1 and 13 have been rejected under 35 U.S.C. 102(e) as being anticipated by Nielsen et al. 5,889,002. Column 14, lines 29-67 and column 15, lines 1-30 are referenced.

Applicants respectfully traverse the rejection. However, in order to advance prosecution, claim 1 has been amended so that e) has been removed and claim 13 has been canceled. Applicants however do reserve the right to file subsequent continuation and/or divisional applications on the cancelled subject matter. In view of the amendment of claim 1 and the cancellation of claim 13, Applicants assert that the rejection of claim 1 has been overcome. Therefore, Applicants respectfully request that the rejection be withdrawn.

**3. The Rejection Under 35 U.S.C. 103**

Claims 1-7, 9-10 and 12-16 have been rejected under 35 U.S.C. 103(a) as being unpatentable over Pirotte et al. 5,459,138 in view of Nielsen et al. US 5,889,002. It is asserted that Pirotte et al. teaches several processes of making pyridino thiadiazine dioxide which include processes a)-d) of the instant claims. It is asserted that Nielsen et al. teaches the equivalency of thieno-fused 1,2,4-thiadiazine dioxide with several heterocyclic ring fused thidiazine dioxide. It is concluded that one having ordinary skill in the art at the time of the invention would have been motivated to combine the teachings of the primary reference with the teachings of the secondary reference.

Applicants respectfully traverse the rejection for a number of reasons. First as acknowledged in the Office Action, the compounds obtained in Pirotte et al. are significantly different from the compounds obtained in the instant application. Second, *contra* to assertions made in the Office Action, the processes used in Pirotte et al. are significantly different as well. In the method of the present invention, nucleophilic substitution is used in a)-d). This is clearly not the case in Pirotte et al. Furthermore, no suggestion was provided in Pirotte et al. that aromatic nucleophilic substitutions was indeed feasible.

Nielsen et al. US 5,889,002 would not be eligible as a prior art reference under 35 U.S.C. 103(a). This is because under 35 U.S.C. 103(c), subject mater which qualifies as prior art only under 35 U.S.C. 102(e), (f) or (g) shall not preclude patentability where there is a common assignee. Both Nielsen et al. and the instant application were assigned to Novo Nordisk. Furthermore, Nielsen et al. is prior art only under 35 U.S.C. 102(e).

Even if Nielsen et al. were prior art, Applicants assert that one of ordinary skill in the art would not be motivated to combine the teachings of Pirotte et al. with Nielsen et al. This is because *contra* to assertions made in the Office Action, the A ring of Nielsen et al. is certainly different from the A ring in formula I of the instant application. Furthermore, there was no teaching of analogous reactions a)-d) in Nielsen et al.

In view of the above arguments, Applicants assert that the rejections under 35 U.S.C. 103 have been overcome. Therefore, Applicants respectfully request that the rejections be withdrawn.

**4. The Double Patenting Rejections**

Claims 1, 13 and 18-23 have been rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-31 of U.S. Patent No. 5,889,002. In response, as noted above, claims 1, 18 and 19 have been amended and claim 13 has been cancelled. Furthermore, as noted above, the A ring of Nielsen et al. is certainly different from the A ring in formula I of the instant application and there was no teaching of

analogous reactions a)-d) in Nielsen et al.

Claims 1, 13, and 18-23 have been rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-25 of U.S. Patent No. 6,329,367. Applicants respectfully traverse the rejection. Again as noted above, claims 1, 18 and 19 have been amended and claim 13 has been cancelled. Additionally, claims 1-24 of U.S. Patent No. 6,329,367 are compound/composition and method of use claims. The compounds recited in claims 18 and 19 can certainly be distinguished from those compounds recited in U.S. Patent No. 6,329,367. The method recited in the instant application is certainly different from the method recited in claim 25 of U.S. Patent No. 6,329,367.

In view of the above arguments, Applicants assert that the obviousness-type double patenting rejections have been overcome. Therefore, Applicants respectfully request that the rejections be withdrawn.

## 6. Conclusions

In view of the above, it is respectfully submitted that all of the pending claims are in condition for allowance. Early action to that end is respectfully requested. The Examiner is hereby invited to contact the undersigned by telephone at (914) 712-0093 if there are any questions concerning this amendment or application.

Respectfully submitted,

Date: 4/24/03

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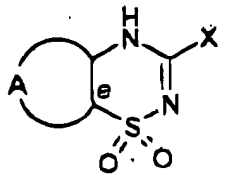
# APPENDIX A



(I)

wherein X is $NR^2R^3$, $SR^1$, $S(=O)R^1$, $S(=O)_2R^1$, or $OR^1$, wherein $R^1$ is hydrogen, $C_{3-6}$-cycloalkyl or ($C_{3-6}$-cycloalkyl)$C_{1-6}$-alkyl the $C_{3-6}$-cycloalkyl group optionally being mono- or polysubstituted with $C_{1-6}$-alkyl, halogen, hydroxy or $C_{1-6}$-alkoxy; a 3-6 membered saturated ring system comprising one or more nitrogen-, oxygen- or sulfur atoms, optionally being mono- or polysubstituted with halogen, cyano, trifluoromethyl, $C_{1-6}$-alkyl, $C_{1-6}$-alkoxy, $C_{1-6}$-alkoxy-$C_{1-6}$-alkyl, aryl, arylalkyl, hydroxy, oxo, nitro, amino, $C_{1-6}$-monoalkyl or dialkylamino; or straight or branched $C_{1-18}$-alkyl, $C_{2-18}$-alkenyl or $C_{2-18}$-alkynyl, each of the groups being optionally mono- or polysubstituted with halogen, hydroxy, $C_{1-6}$-alkoxy, $C_{1-6}$-alkylthio, $C_{3-6}$-cycloalkyl, nitro, amino, $C_{1-6}$- monoalkyl- or dialkylamino, cyano, oxo, formyl, acyl, carboxy, $C_{1-6}$-alkoxycarbonyl, carbamoyl, formylamino, $C_{1-6}$-alkylcarbonylamino, aryl, aryloxy, arylalkoxy; bicycloalkyl, aryl, heteroaryl, arylalkyl or heteroarylalkyl, each of the groups being optionally mono- or polysubstituted with halogen, hydroxy, $C_{1-6}$-alkyl, $C_{1-6}$-alkoxy, aryloxy, arylalkoxy, nitro, amino, $C_{1-6}$-monoalkyl- or dialkylamino, cyano, oxo, acyl or $C_{1-6}$-alkoxycarbonyl;

$R^2$ is hydrogen; hydroxy; $C_{1-6}$-alkoxy; or $C_{1-6}$-alkyl, $C_{3-6}$-cycloalkyl, $C_{2-6}$- alkenyl or $C_{2-6}$-alkynyl optionally mono- or polysubstituted with halogen;

$R^3$ is hydrogen, $C_{3-6}$-cycloalkyl or ($C_{3-6}$-cycloalkyl)$C_{1-6}$-alkyl, the $C_{3-6}$-cycloalkyl group optionally being mono- or polysubstituted with $C_{1-6}$-alkyl, halogen, hydroxy or $C_{1-6}$-alkoxy; a 3-6 membered saturated ring system comprising one or more nitrogen-, oxygen- or sulfur atoms; or straight or branched $C_{1-18}$-alkyl optionally mono- or polysubstituted with halogen, hydroxy, $C_{1-6}$-alkoxy, $C_{1-6}$-alkylthio, $C_{3-6}$-cycloalkyl, aryl, aryloxy, arylalkoxy, nitro, amino, $C_{1-6}$-monoalkyl- or dialkylamino, cyano, oxo, formyl, acyl, carboxy, $C_{1-6}$-alkoxycarbonyl, or carbamoyl;

or $R^3$ is $-OR^4$; $-C(=Z)R^4$; $-NR^4R^5$; bicycloalkyl, aryl, heteroaryl, arylalkyl or heteroarylalkyl optionally mono- or polysubstituted with halogen, hydroxy, $C_{1-6}$-alkyl, $C_{1-6}$-alkoxy, aryloxy,

arylalkoxy, nitro, amino, $C_{1-6}$-monoalkyl- or dialkylamino, cyano, oxo, acyl or $C_{1-6}$-alkoxycarbonyl;

wherein $R^4$ is hydrogen; $C_{3-6}$-cycloalkyl or ($C_{3-6}$-cycloalkyl)$C_{1-6}$-alkyl, the $C_{3-6}$-cycloalkyl group optionally being mono- or polysubstituted with $C_{1-6}$-alkyl, halogen, hydroxy or $C_{1-6}$-alkoxy; a 3-6 membered saturated ring system comprising one or more nitrogen-, oxygen- or sulfur atoms; or straight or branched $C_{1-18}$-alkyl optionally mono- or polysubstituted with halogen, hydroxy, $C_{1-6}$-alkoxy, $C_{1-6}$-alkylthio, $C_{3-6}$-cycloalkyl, aryl, aryloxy, arylalkoxy, nitro, amino, $C_{1-6}$-monoalkyl- or dialkylamino, cyano, oxo, formyl, acyl, carboxy, $C_{1-6}$-alkoxycarbonyl, or carbamoyl;

Z is O or S;

$R^3$ is hydrogen; $C_{1-6}$-alkyl; $C_{2-6}$-alkenyl; $C_{3-6}$-cycloalkyl optionally mono- or polysubstituted with $C_{1-6}$-alkyl, halogen, hydroxy or $C_{1-6}$-alkoxy;
or, when or $R^3$ is $-NR^4R^5$, $R^4$ and $R^5$ together with the nitrogen atom form a 3-12 membered mono- or bicyclic system, in which one or more of the carbon atoms may be exchanged with nitrogen, oxygen or sulfur, each of these ring systems optionally being mono- or polysubstituted with halogen, $C_{1-6}$-alkyl, hydroxy, $C_{1-6}$-alkoxy, $C_{1-6}$-alkoxy-$C_{1-6}$-alkyl, nitro, amino, cyano, trifluoromethyl, $C_{1-6}$-monoalkyl- or dialkylamino, oxo;

or, when X is $NR^2R^3$, $R^2$ and $R^3$ together with the nitrogen atom form a 3-12 membered mono- or bicyclic system, in which one or more of the carbon atoms may be exchanged with nitrogen, oxygen or sulfur, each of these ring systems optionally being mono- or polysubstituted with halogen, $C_{1-6}$-alkyl, hydroxy, $C_{1-6}$-alkoxy, $C_{1-6}$-alkoxy-$C_{1-6}$-alkyl, nitro, amino, cyano, trifluoromethyl, $C_{1-6}$-monoalkyl- or dialkylamino or oxo;

*A* together with the carbon atoms forming bond *e* of formula I represents a 5 membered heterocyclic system comprising one or more nitrogen-, oxygen- or sulfur atoms, the heterocyclic systems optionally being mono- or polysubstituted with halogen; $C_{1-18}$-alkyl; $C_{3-6}$-cycloalkyl; hydroxy; $C_{1-6}$-alkoxy; $C_{1-6}$-alkoxy-$C_{1-6}$-alkyl; nitro; amino; cyano; cyanomethyl; perhalomethyl; $C_{1-6}$-monoalkyl- or dialkylamino; sulfamoyl; $C_{1-6}$-alkylthio; $C_{1-6}$-alkylsulfonyl; $C_{1-6}$-alkylsulfinyl; $C_{1-6}$-alkylcarbonylamino; arylthio, arylsulfinyl, arylsulfonyl, aryl, arylalkyl, aryloxy, the aryl group optionally being mono- or polysubstituted with $C_{1-6}$-alkyl, perhalomethyl, halogen, hydroxy or $C_{1-6}$-alkoxy; $C_{1-6}$-alkoxycarbonyl; $C_{1-6}$-alkoxycarbonyl-$C_{1-}$

$_{6}$-alkyl; carbamyl; carbamylmethyl; $C_{1-6}$-monoalkyl- or dialkylaminocarbonyl; $C_{1-6}$-monoalkyl- or dialkylaminothiocarbonyl; ureido; $C_{1-6}$-monoalkyl- or dialkylaminocarbonylamino, thiocarbamyl; thioureido; $C_{1-6}$-monoalkyl- or dialkylaminothiocarbonyl- amino; $C_{1-6}$-monoalkyl- or dialkylaminosulfonyl; carboxy; carboxy-$C_{1-6}$-alkyl; acyl; formyl; or a 5 - 6 membered nitrogen, oxygen or sulfur containing ring, optionally substituted with $C_{1-6}$-alkyl or phenyl, the phenyl group optionally being mono- or polysubstituted with $C_{1-6}$-alkyl, perhalomethyl, halogen, hydroxy or $C_{1-6}$-alkoxy;

or a salt thereof with a pharmaceutically acceptable acid or base.

Within its scope the invention the process for preparation of compounds of formula I includes all optical isomers of compounds of formula I, some of which are optically active, and also their mixtures including racemic mixture thereof.

The scope of the invention also includes all tautomeric forms of the compounds of formula I as well as metabolites or prodrugs of a compound of formula I.

The salts include pharmaceutically acceptable acid addition salts, pharmaceutically acceptable metal salts or optionally alkylated ammonium salts, such as hydrochloric, hydrobromic, hydroiodic, phosphoric, sulfuric, trifluoroacetic, trichloroacetic, oxalic, maleic, pyruvic, malonic, succinic, citric, tartaric, fumaric, mandelic, benzoic, cinnamic, methanesulfonic, ethanesulfonic, picric and the like, and include acids related to the pharmaceutically acceptable salts listed in Journal of Pharmaceutical Science, 66, 2 (1977) and incorporated herein by reference, or lithium, sodium, potassium, magnesium and the like.

A "metabolite" of a compound disclosed in this application is an active derivative of a compound disclosed herein which is produced when the compound is metabolized. Metabolites of compounds disclosed herein can be identified either by administration of a compound to a host and an analysis of blood samples from the host, or by incubation of compounds with hepatic cells in vitro and analysis of the incubant. A "prodrug" is a compound that either is converted into a compound disclosed in the application in vivo or has the same active metabolite as a compound disclosed in this application.

The term "$C_{1-6}$-alkoxy" as used herein, alone r in combination, refers to a straight or